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Birch reduction of benzenesulfonamide and benzenephosphonic acid

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BIRCH REDUCTION OF BENZENESULFONAMIDE AND BENZENEPHOSPHONIC ACID

A Thesis

Presented to

the Faculty of the Graduate School

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Master of Science

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by

Tony Ping-Fong Niem

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INTRODUCTION

The use of an alkalai metal dissolved in liquid ammonia and a proton source such as alcohol to effect partial reduction of aromatic compounds, commonly known as the Birch reduction, has proven to be a synthetic procedure of great utility. (1) The flexibility and usefulness of this reaction has attracted increasing attention in recent times, primarily by Birch (1,2) The overall reaction occruing during the Birch reduction of benzene is indicated by Figure 1.

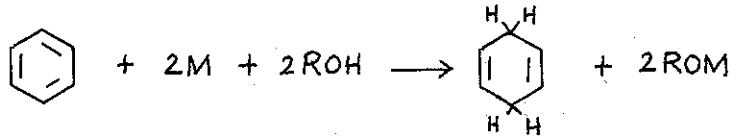


Figure 1

Birch has suggested that the reaction may proceed by the transfer of one electron to the aromatic nucleus to give a radical anion or a transfer of two electrons to form a dianion. (2,3,4) Either intermediate would then be a very strong base and would react promptly with proton donors such as alcohols, water, or ammonium salts. Figure 2

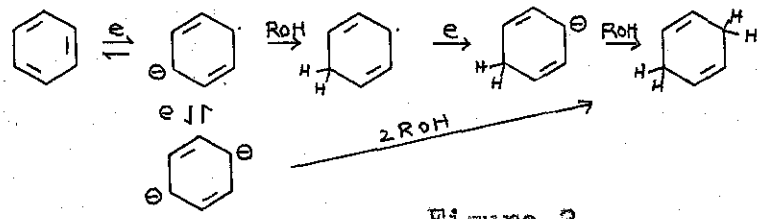


Figure 2

An investigation (5) of the kinetics of the metal-ammonia-alcohol reduction of benzene has shown that the reduction is third order, being first order with regard to each component (metal, alcohol, benzene.) The rate law may be expressed as:

$$-d(ArH)/dt = k(ArH)(M)(ROH)$$

Figure 3

where (ArH) is the concentration of aromatic hydrocarbon, (M) the concentration of metal and (ROH) the concentration of alcohol. This kinetic study is consistant with the radical anion mechanism proposed by Birch. Polynuclear aromatic compounds most likely go via a dianion path (4) as evidenced by the isolation of disodium dianion of phenanthrene, anthracene and naphthalene.

A less generally accepted mechanism for Birch reduction has been proposed by Huckel and Co-workers (6). They suggest that the first step in the reduction of benzene in liquid ammonia may involve the addition of a hydrogen atom. Figure 4

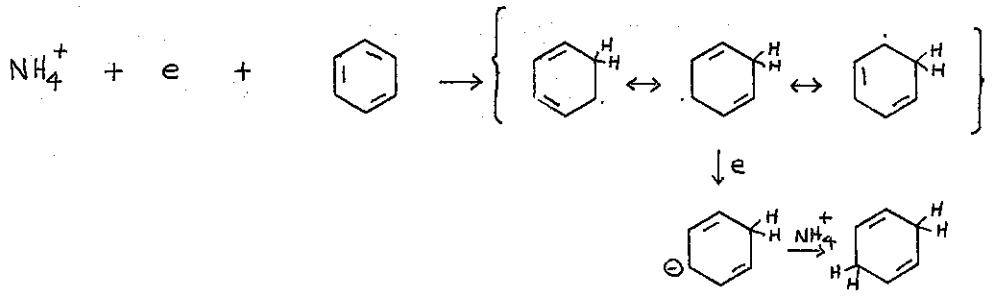


Figure 4

(The atomic hydrogen is postulated as being released as the result of a three body collison, perhaps between an ammonium ion, a benzene molecule and a electron. The ammonium ion is formed from ammonia and a proton supplied by the "acid" and is stablized by solvation.) This would be followed by the addition of an electron to give an anion which would then quickly accept a proton to give the dihydrobenzene. The observed kinetic evidence (5) is also in agreement with Huckel's theory.

In radical anion mechanism Figure 5, the equilbrium involving the initial electron addition must favor the left hand side because of the unfavorable resonance energy change involved in the formation of Ar^{*-}. Since no reduction of benzene is believed to occur in the absence of a proton source, it appears that no reduction can ensue unless this anion radical is rapidly and irreversibly protonated to ArH.(8) Ammonia apparently cannot provide the necessary proton

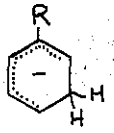
$$Ar + e \rightleftharpoons Ar^{*-} \xrightarrow{ROH} ArH^{*} + e \longrightarrow ArH^{\ominus} \xrightarrow{ROH} ArH_2$$

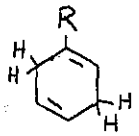
Figure 5

because of its low acidity ($pk_a = 34$) but alcohols (pk_a 16-18) can do so. Subsequent stages from ArH^{*} may be rapid and are probably irreversible.

The radical anion mechanism can be used to predict correctly the nature of the principal reduction products from monobenzoid hydrocarbon and from anisoles and anilines, as

follows.(8) The structures of the dihydrobenzenes will be determined by two factors. (i) The position of addition of the first proton to the anion radical Ar^{*-} and (ii) the position of addition of the second proton to the mesomeric anion ArH^{-}. The expectation is that addition to Ar^{*-} should occur in the position of greatest free charge density; i.e. meta to an o, p-directing substituent, since accumulation of charge in the ortho and para positions will be opposed by the substituent. Thus with, say, toluene, anisole and dimethylaniline, addition of the second electron to the radical ArH^{*} should give the mesomeric anion Figure 6





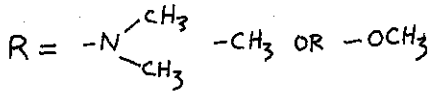


Figure 6 Figure 7

For irreversible proton addition, the products will be determined by relative rates of combination of the proton with the positions in the anion where free charge can appear; i.e. the reaction will be kinetically controlled. The predominant product will then be that formed by addition at the position of greatest free charge density which is in the middle of the mesomeric system (9) and correspond to the 2-position Figure 6. Accordingly a kinetically controlled

addition of a proton to the anion Figure 6 would be predicted to give the unconjugated isomer Figure 7. All this assumes that any steric effect of substituent is negligible.

With two substituents addition would be expected meta to the most strongly o, p-directing group, preferably not in a position carrying an o, p-directing group. Thus, p-xylene is reduced to 2,5-dihydro-p-xylene Figure 8 and o-and m-xylene give a mixture of two possible isomers. However, the predominant isomer is that formed by hydrogen addition to the unsubstituted position.

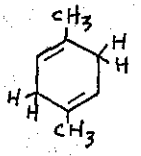


Figure 8

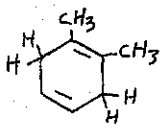


Figure 9

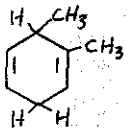


Figure 10

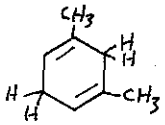


Figure 11

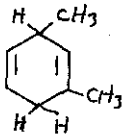


Figure 12

O-xylene is reduced to 3,6-dihydro-o-xylene Figure 9 and 1, 4-dihydro-o-xylene Figure 10. M-xylene is reduced to 2,5-dihydro-m-xylene Figure 11 and 1,4 dihydro-m-xylene. Figure 12.

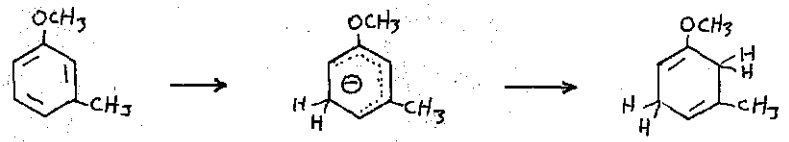


Figure 13 Figure 14

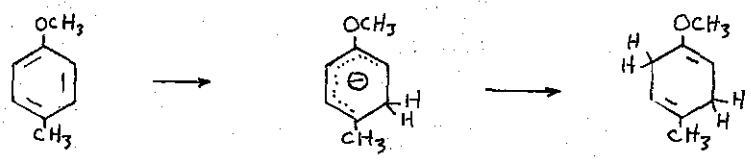


Figure 15 Figure 16

3-methylanisole Figure 13 and 4-methyl-anisole Figure 15 are reduced to 2,5-dihydro-3-methylanisole Figure 14 and 3,6-dihydro-4-methylanisole Figure 16 respectively (2). 2-methy-anisole Figure 17 is reduced to 2, 5- and 3, 6-dihydro-2-methylanisole, Figure 18, 19 in which the latter predominates (7)

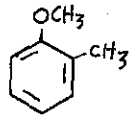


Figure 17

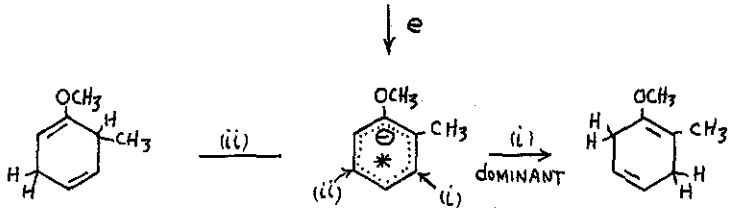


Figure 18 Figure 19

Substitution of a benzene nucleus with electron-releasing groups (such as alkyl group and amino group; methoxyl group is an exception) in general decrease these ease of Birch reduction (4,10) and give 2,5-dihydroderivatives.

The substitution with electron withdrawing groups (such as carboxyl and amide groups) activate the benzene nucleus for reduction, and gives 1,4-dihydroderivatives (10,11) for these groups can stablize the negative charges through resonance structures. Figure 20 (1)

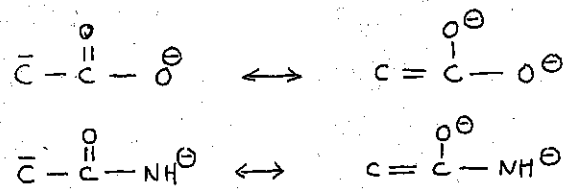


Figure 20

In reduction of benzoic acid, the dianion Figure 21 is believed to be formed before protonation, since 1,4-dihydrobenzoic acid is formed even in the absence of alcohol.(18)

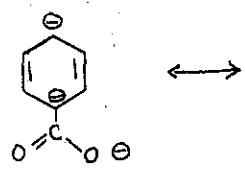


Figure 21

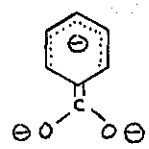


Figure 22

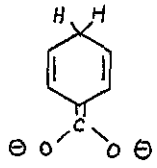


Figure 23

In the dianion Figure 21, the anionic charges are located <u>para</u> to one another by their mutual repulsion and in the 1,4-positions by the stablization of one charge by the carboxylate group Figure 22. Protonation of the resulting anion at the carbon position of greatest free charge density would then give the mesomeric anion Figure 23. The protonation of such anion is kinetically controlled giving the 1,4-dihydrobenzoic acid (10,11). Likewise, <u>o</u>-toluic acid Figure 24 gives the 1, 4-dihydro-<u>o</u>-toluic acid Figure 25 on reduction (12)

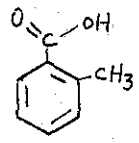


Figure 24

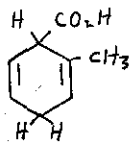


Figure 25

However, p-toluic acid gives a tetrahydroacid (11). This result has been reasonably rationalized on the assumption that in the dianion, formed by the addition of two electrons to the p-toluate anion, there is a choice of having maximum charge density at a tertiary or a secondary carbon. Since a secondary carbanion, Figure 27, is favored over a tertiary carbanion, Figure 26, one can expect an increase of charge density meta to the methyl-substituted carbon and a decrease of charge density at that tertiary position. Thus protonation of dianion, Figure 27 gives the product, Figure 28 containing conjugated double bonds which then undergo further reduction (10,11).

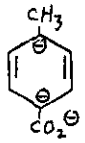


Figure 26

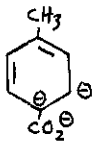


Figure 27

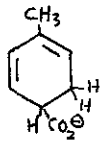


Figure 28

O-anisic acid is reduced to 1,4-dihydro-2-methoxybenzoic acid, Figure 29 on Birch reduction (13)

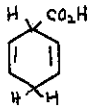


Figure 29

Benzamide, Figure 30 with sodium end ethanol in liquid ammonia is reported (14) to give mainly toluene, Figure 31. Thus instead of reduction of the aromatic ring, reduction of the amide group to a benzylic alcohol occured followed by reductive cleaveage to the methyl compound.

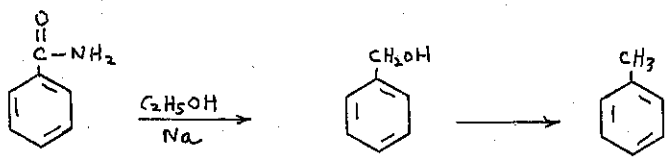


Figure 30 Figure 31

The amides differ from the carboxylic acids in that they lead to anions of higher energy or, in other words, amides are less acidic. Substituents that would help to stablize the amide anion could make the amide sufficiently acidic to form its anion and thus render it immune to reduction. Thus m-methoxybenzamide is reported (11) to be reduced to 1,4-dihydro-3-methoxybenzamide, Figure 32 when subjected to excess of sodium in ammonia and ethanol. Excess of sodium must be used to satisfy the side reaction of sodium and ethanol, which occurs at a comparable rate. 3,5-dimethoxybenzamide is reported (11) to be reduced to 1,4-dihydro-3,-5-dimethoxybenzamide, Figure 33.

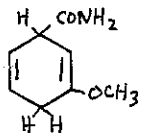


Figure 32

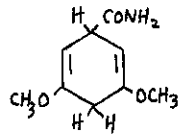


Figure 33

The reduction of benzamide to 1,4-dihydrobenzamide, Figure 34 was achieved in high yield by using t-butylalcohol in place of ethanol (11). By using this less acidic proton source, stablization of the amide as its anion, Figure 35 apparently was possible and the rate of the competing reduction of the amide group itself was slowed (11).

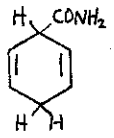


Figure 34

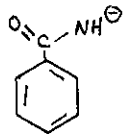


Figure 35

As in the cases of benzoic acid and benzamide, Benzenesulfonamide and benzenephosphonic acid also have electron withdrawing groups and form anions in basic solution. Therefore, it is expected that they would also be reduced to 1,4-dihydroderivatives instead of 2,5-dihydroderivatives. This thesis is a report of the examination of the Birch reduction of these two compounds.

RESULTS AND DISCUSSION

In benzenesulfonamide, Figure 36, the deactivating effect of the sulfonamide group in electrophilic substitution reaction is usually attributed to electron attractive effects which result from inductive, Figure 37 and mesomeric, Figure 38 factors. Mesomeric consideration indicates that the ortho and para positions are more electron deficient than meta position (15)

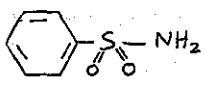


Figure 36

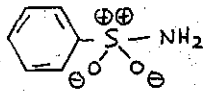


Figure 37

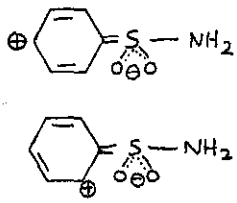


Figure 38

This effect of resonance is revealed in the marked bathochromic influence on the ultraviolet spectrum of benzene which is exerted by sulfonamide group (30). Similarly the electron withdrawing effect of a sulfonamide group would be expected to activate the benzene nucleus for Birch reduction, since an addition of an electron to the ring is involved. In terms of radical anion mechanism, Figure 2, the expectation would be that the addition of the first proton to anion radical should occur in the position of greatest free charge density in the ring; i.e. ortho or para to the sulfonamide substituent. Thus with benzenesulfonamide, addition of second electron to the radical ArH^{*} should give the mesomeric anion, Figure 39.

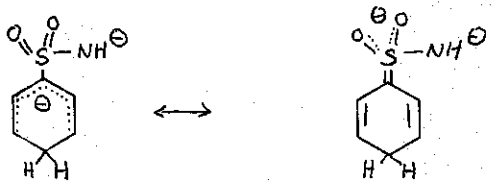


Figure 39

Figure 40

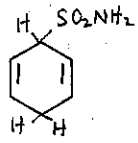


Figure 41

The protonation of such anions in liquid ammonia is apparently kinetically controlled (12) since the less stable, non-conjugated diene systems are produced. Addition should occur at point of greatest free charge density which is located in the middle of mesomeric system (9) stablized by the sulfonyl group and corresponds to 1-position, Figure 39. Thus one would result rather than 2,5-isomer.

In terms of dianion mechanism, Figure 2, the anionic charges are located <u>para</u> to one another by their mutual repulsion and in the 1,4-positions by the stablization of one charge by the sulfonamide group (11). Protonation of the resulting anion, Figure 42 at the carbon position of greatest free charge density should give the mesomeric anion, Figure 43. The protonation of such anion is expected to be kinetically controlled (12), giving the 1, 4-dihydrobenzenesulfonamide, Figure 41.

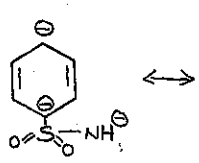


Figure 42

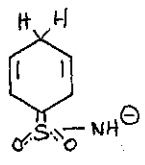


Figure 43

In connection with protection of amide groups, a comparison of acidity of benzenesulfonamide with that of benzoic acid and benzamide would be helpful.

TABLE I

PKa VALUES

	PK_a (16)
Benzoic acid	4.5
Benzamide	15-16
Benzenesulfonamide	10
Ethanol	18
t-butanol	19

Thus the order of acidity is as follows:

$$\phi CO_2H > \phi SO_2NH_2 > \phi CONH_2$$

Benzoic acid is highly acidic, therefore, the carboxylic acid group is in the anion form and is protected during Birch reduction (11). The amide group of the benzamide has been reported (11) reduced by Birch reduction when ethanol is used. This may be that since benzamide is very weakly acidic, it is not in the anion form, and hence it is not protected. (Experimental result of the present investigation contradicts the above reported reduction of the amide group with ethanol as the

TABLE II

BIRCH REDUCTION OF BENZENESULFONAMIDE

	Lithium	Alcohol	Benzene-Sulfonamide	Experimental Condition	Product
I	2.8g (.4 mole) Excess	65 ml Ethanol	7.4g (.05 mole)	Add lithium first, then add Ethanol. Dry Liquid NH_3	Thiophenol 65% Diphenyldisulfide 9%
II	2.8g (.4 mole) Excess	65 ml Ethanol	7.4g (.05 mole)	Add Ethanol first then add lithium	No reduction
III	2 g (.27 mole) Equivalent Amount	100 ml Ethanol	12.9g (.082 mole)	Add lithium first, then add Ethanol	Thiophenol 68% Diphenyldisulfide 6.4%
IV	2.8g (.4 mole) Excess	100 ml tert-butyl alcohol	7.4g (.05 mole)	Add lithium first, then add tert-butanol Dry Liquid NH_3	Thiophenol 69% Diphenyldisulfide 6.9%
V	2.8g (.4 mole) Excess	100 ml tert-butyl alcohol	7.4g (.05 mole)	Add Tert-Butanol first, then add lithium	No reduction
VI	2 g (0.27 mole) Equivalent Amount	100 ml tert-butyl alcohol	12.9 g (.082mole)	Add lithium, Then add tert-butanol	Thiophenol 62.5% Diphenyedisulfide 8%

proton source. This will be discussed in detail later in the discussion. However, when less acidic tert-butanol is used as proton source, reduction of the ring instead of amide group has been reported (11). Thus it appears that when benzamide is in anionic form as is benzoic acid, the functional group is protected, and reduction of the ring occurs. When benzamide is not in the anionic form, the amide group is reduced instead of the ring. Since benzenesulfonamide is more acidic than benzamide, its anion stablization would be predicted to protect the functional group when either tert-butanol or ethanol is used as proton source.

In the attempt to reduce the ring of benzenesulfonamide, six variations in experimental conditions are made. (See Table II.)

"Dry" liquid ammonia was used in experiments (I) and (IV). (It was dried by refluxing the liquid ammonia with lithium in a three necked flask and then it was distilled into the reaction flask.) The absence of water in liquid ammonia eliminated the possibility that any reduction of sulfonamide group might be due to water as the proton source. It was important to be sure of this point since water is more acidic than either tertiary butanol or ethanol and since the acidity of the proton source had been reported to be quite critical in the case of benzamide (11) where ethanol gave

reduction of the amide group and tert-butyl alcohol gave reduction of the ring.

In experiments (II) and (V), no reduction occurs. Apparently lithium added reacted faster with ethanol to form lithium ethoxide instead of causing reduction of benzene-sulfonamide. In experiments (I), (III), (IV) and (VI), benzenewulfonamide, Figure 44 is reduced to mainly thiophenol, Figure 45, and diphenyldisulfide, Figure 46 in minor quantity.

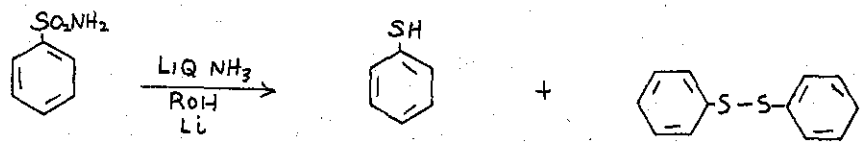
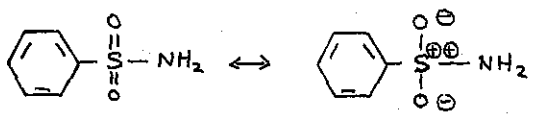


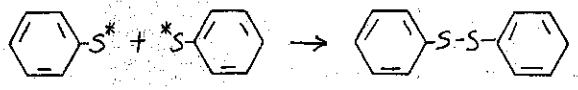
Figure 44 Figure 45 Figure 46

Thus reduction of the functional group occurs instead of reduction of the ring. The sulfonamide group is probably very easily reduced in comparison with carboxyamide group. It would be interesting to carry out experiments to determine the relative rates of reduction of methanesulfonamide and acetamide. In this manner, the direct comparison of the ease of reduction of these functional groups could be made. The ease of reduction of the sulfonamide group may be due to the fact that from the structures



the electron deficiency of the sulfur atom may allow it to accomodate electron easily.

Diphenyldisulfide might be formed by dimerization of a phenylsulfur radical:



Alternatively it may be formed by the direct oxidation of thiophenol.

It has been reported that N-toluene-p-sulphonyl derivatives of amino acids have been cleaved to the amino acids by sodium in liquid ammonia, Figure 47 (19,20)

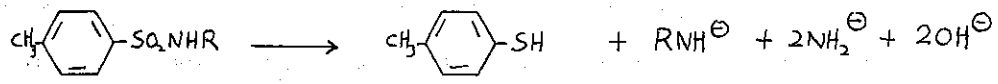


Figure 47

Here, the electron donating properties of the methyl group as well as the steric hindrance of attack of protonating agent at para position would be expected to substantially reduce the rate of reduction of the ring.

In contrast to the reduction of benzamide which was reported (11) to give reduction of the ring with tert-butyl alcohol, reduction of benzenesulfonamide in present investigation gave reduction of the sulfonamide group, when tert-butyl alcohol was used as proton source. Therefore, re-investigation of reduction of benzamide was necessary in order to see whether with present experimental techniques, it was able to reproduce the experimental results which were reported (11), (i.e. reduction of the ring with tert-butyl alcohol). However,

it was found in the present investigation that reduction of the ring rather than amide group of benzamide took place even with ethanol and "wet" ammonia in contradiction to the literature report (11). Therefore, it was not necessary to use dry liquid ammonia and tert-butyl alcohol conditions. Of course, the present experimental conditions were somewhat different. Here, lithium was used instead of sodium; also the order of addition of reagents was reversed. Lithium was added first and then ethanol in the present study. A more thorough investigation of the effect of the above experimental conditions would be required before one could reach any conclusions about the conflicting results of the present investigation and those previously reported (11).

In the attempt to reduce the ring of benzenephosphonic acid, five variations in experimental conditions were made. (See Table III.) However, no reduction of the compound apparently occured and only starting material was isolated in each experiment. An attempt is made here to explain this unusual situation.

From ultraviolet study of benzenephosphonic acid (21), it is found that the phosphono group causes no profound change in the general characteristics of the spectrum of the present compound. The spectrum of phosphorous compound is shifted less than 10 mu to the longer wave-length and the intensity of absorption is increased by a factor between 1.5 and 4.

TABLE III

BIRCH REDUCTION OF BENZENEPHOSPHONIC ACID

Lithium	Ethanol	Benzene-phosphonic Acid	Experimental Condition	Product
4.5g (0.64 mole) Excess	100 ml	12.6g (0.08 mole)	Add lithium first, then add Ethanol	No reduction 90% recovery
4.5g (0.64 mole) Excess	100 ml	12.6g (0.08 mole)	Add Ethanol first, then add Lithium	No reduction 85% recovery
2.25g (0.32 mole) Equivalent amount	100 ml	12.6g (.08 mole)	Add lithium first, then add ethanol	No reduction
4.5g (0.64 mole) Excess	100 ml	12.6g (.08 mole)	Use Diethyl ether as co-solvent. Add lithium first then ethanol	No reduction 85% recovery
4.5g (0.64 mole) Excess	100 ml	12.6g (0.08 mole)	Use tetra-Hydrofuran as co-solvent. Add lithium first, then add ethanol	No reduction 83% recovery

The vibrational structure is virtually unaltered. The effects of the $-PO_3H^-$ and the $PO_3^=$ groups are reported (21) even less than that of the phosphono group. A benzene derivative with considerable resonance between group and ring has an ultraviolet absorption spectrum which differs markedly from that of the parent hydrocarbon. A purely inductive substituent on the other hand produces little intensification of the absorption (22). The relatively small effect of the phosphono group suggests that no appreciable resonance exists between this group and the aromatic nucleus (21). Therefore, it is probable that the phosphorous atom of this substituent has no π-orbitals which can interact with the π-electrons of the benzene ring. This conclusion is consistent with the view that the P-O bond of the phosphoryl group has no appreciable double bond character, Figure 48.

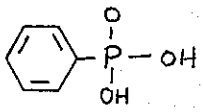


Figure 48

Benzenephosphonic acid undergo the usual aromatic substitutions with the apparently exclusive substitution in the meta position of the benzene ring (23,24.). Thus the meta-directing effect of the phosphono group in electrophilic substitution reaction is attributed to the electron attractive effect

which results from inductive factor only since little or no resonance interaction exists between the phosphono group and the benzene ring as indicated by ultraviolet studies (21). Inductive consideration indicates that ortho and para positions are more electron deficient than meta position, Figure 49. However, the substituent $-PO_3H^-$ is only weakly

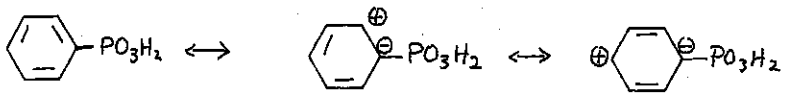


Figure 49

electron attracting in both meta and para position, and the substituent $-PO_3^=$ is electron repelling in both positions (25). These properties were found experimentally by studying the effect of these groups on the acidity of some acidic function in aromatic compounds. The data in table (IV) permit calculation of substituent constants (σ) for the groups PO_3H^- and $PO_3^=$ and is shown in table (V). Positive σ value indicates the group being electron attracting and the negative value indicates it being electron-repelling.

The fact that phosphono dianion $PO_3^=$ is electron repelling in both meta and para positions (25) provides basis for an explanation as to why the Birch reduction doesn't occur with benzenephosphonic acid since electrons added to the meta or para position would be destablized by the electron

TABLE IV

PK'S OF ACIDIC FUNCTIONS

Compound	PK in H_2O	PK in 50% EtOH
p-HOOC $C_6H_4PO_3H^-$	3.95	5.36
m-HOOC $C_6H_4PO_3H^-$	4.03	5.29
m-$Et\overset{+}{N}H_2C_6H_4PO_3H^-$	4.90	
m-$Me\overset{+}{N}H_2C_6H_4PO_3H^-$	4.71	
p-$HOC_6H_4PO_3^=$	9.9	10.9
m-$HOC_6H_4PO_3^=$	10.2	12
p-$NH_2SO_2C_6H_4PO_3^=$	10.0	11.1
p-$NH_3^+(CH_2)_2OC_6H_4PO_3^=$	9.5	

TABLE V

Substituent Constants of the Phosphono anions

Substituent	Meta	Para
PO_3H^-	0.25, 0.24	0.17, 0.29
$PO_3^=$	-0.02	-0.16

repelling PO_3 group. The lack of double bond character of phosphoryl group, that is lack of following structures, Figure 50,

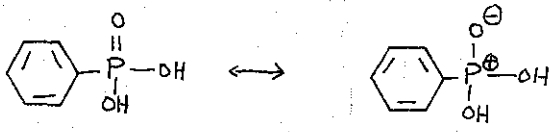


Figure 50

perhaps explains why the phosphono group itself is also not reduced since addition of electrons is not probable due to low electron affinity of phosphorous atom here (21).

Since benzenephosphonic acid does not seem to be too soluble in liquid ammonia, this lack of solubility could be responsible for the lack of reduction. In two experiments, tetrahydrofuran and diethyl ether were used as co-solvents in order to increase the solubility of benezenephosphonic acid in liquid ammonia. However, no reduction occurred. But the possibility remains that diethyl ether and tetrahydrofuran might be inefficient as a co-solvent for this particular compound although they alone do dissolve benzenephosphonic acid. By adding alcohol slowly, any small amount of benzene-phosphonic acid which is present in solution, should be reduced and be replaced by more benzenephosphonic acid going into the solution. An attempt was made by adding alcohol very slowly, but still no reduced product was found.

It was reported (11) that 1,4- dihydrobenzoic acid was purified by vacuum distillation at an elevated temperature. Another method of purification of this acid was made here by making a solid derivative of the acid with benzylthiourea. The derivative was then purified by repeated crystallization and converted back to the free acid.

A new derivative of 1,4-dihydrobenzoic acid was made by treating the acid with p-bromophenacyl bromide to form an ester.

SUMMARY

1. By using different experimental conditions of Birch reduction, benzenesulfonamide was reduced in each case to thiophenol and diphenyldisulfide.

2. By using different experimental conditions of Birch reduction, benzenephosphonic acid did not subject to reduction in each case.

3. a. A new derivative, p-bromophenacyl ester, of 1, 4-dihydrobenzoic acid was made.

b. A method of purification of 1, 4-dihydrobenzoic acid was made by making a solid derivative of 1, 4-dihydrobenzoic acid with benzylthiourea. The derivative was purified and converted back to free acid. This method of purification replaces purification by vacuum distillation.

4. In contrast to what has been reported, benzamide was reduced to 1, 4-dihydrobenzamide when ethanol was used as proton source.

EXPERIMENTAL

(A) Reduction of Benzenesulfonamide

(1) First Attempt of Reduction of Benzenesulfonamide.

Seven and four-tenth gram (0.05 mole) of benzenesulfonamide (Eastman Kodak) was added to 600 ml of dry liquid in a two liter three-necked flask equipped with a mechanical stirrer, a dropping funnel and a dry ice condenser. (The liquid ammonia was dried by refluxing the liquid ammonia with lithium for an hour in a 2 liter three-necked flask with stirring. It was then distilled under warm water bath into another 2 liter three-necked flask.) The solution was stirred while 2.8 g (0.4 mole) of lithium was added in small pieces over 15 minutes. Then 65 ml of anhydrous ethanol was added over a period of 45 minutes with stirring; followed by addition of 21.4 g (0.4 mole) of ammonium chloride. The ammonia was allowed to evaporate and the residual material dissolved in 200 ml of ice water. After acidification with 10% hydrochloric acid, the solution was extracted with four 100 ml portions of ether. The combined ether solution was dried over magnesium sulfate. The ether solution was concentrated by distillation under vacuum to remove ether and ethanol. The remaining liquid was distilled at 168° - 169° giving 3.6 g (65%) of light yellow liquid. This liquid was

thiophenol as indicated by ultraviolet absorption at 235 mu and infrared spectrum which was same as that was recorded for that compound (31). The residue left after distillation was crystallized from ethanol and water giving 0.59 g (9%) of diphenyldisulfide. The compound was diphenyldisulfide as indicated by ultraviolet absorption at λ_{max} 240 mu and infrared spectrum which was same as that was recorded for that compound (32,33).

(II) Second Attempt

Same quantities of reagents were used here as in experiment (I). This time, added ethanol first over a period of 20 minutes. Then added lithium in small pieces over 30 minutes, followed by ammonium chloride. The isolation procedure was as described above. Distillation of ether gave 6.9 g of solid residue. After crystallized from ethanol, it melted at 152°C. Melting point, ultraviolet and infrared data indicated it was original compound.

(III) Third Attempt

The procedure was same as experiment (I) using 12.9 g (0.082 mole) of benzenesulfonamide, 2 g (0.27 mole) of lithium and 100 ml of ethanol. The liquid portion (6 g or 68%) isolated was shown to be thiophenol and the solid portion (0.56 g or 6.4%) was shown to be diphenyldisulfide from spectral data.

(IV) Fourth Attempt.

Seven and four-tenth gram of benzenesulfonamide was added to 600 ml liquid ammonia. 2.8 g (0.4 mole) of lithium was added over 20 minutes. This time, 100 ml of anhydrous tert-butanol was added over 45 minutes followed by 21.4 g (0.4 mole) of ammonium chloride. The isolation procedure was as before. The liquid portion (3.8 g or 69%) isolated was shown to be thiophenol and the solid portion (0.38 g or 6.8%) was shown to be diphenyldisulfide from spectral data.

(V) Fifth Attempt.

Same quantities of reagents were used here as in experiment (IV). This time added tertiary butanol first over 25 minutes. Then added lithium in small pieces over 30 minutes, followed by ammonium chloride. The isolation procedure was as described for experiment (II). Only solid residue (7.1 g) was isolated and was shown to be the original compound from melting point, ultraviolet and infrared data.

(VI) Sixth Attempt.

The procedure was same as experiment (IV) using 12.9 g (0.082 mole) of benzenesulfonamide, 2 g (0.27 mole) of lithium and 100 ml tertiary butanol. The liquid portion (5.5 gm or 62.5%) isolated was shown to be thiophenol and solid portion (0.79 or 8%) was shown to be diphenyldisulfide from spectral data.

(B) Reduction of Benzamide.

(I) Fifteen gram (0.124 mole) of benzamide was added to 600 ml of liquid ammonia in a 2 liter three-necked flask. The solution was stirred while 3 g (0.42 mole) of lithium was added in small pieces over 20 minutes. Then 150 ml of absolute ethanol was added over 30 minutes followed by 30 g (0.56 mole) of ammonium chloride. The ammonia was allowed to evaporate and the residual material dissolved in 150 ml of ice water. After acidification with 10% hydrochloric acid, the solution was extracted with four 100 ml portions of ether. The combined ether solution was dried over magnesium sulfate. The ether solution was distilled under vacuum to dryness to give 8.9 g (59%) of residue. After three recrystallization from benzene, 3.2 g of 1, 4-dihydrobenzamide m.p. 149 - 152° C was obtained. The material showed only end absorption in the ultraviolet and no maximum at 224 mu. The infrared spectrum also indicated lack of absorption in aromatic double bond region.

(II) Hydrogenation of 1,4 dihydrobenzamide.

A solution of 1.5 of this 1,4-dihydroderivative in 30 ml of ethanol was hydrogenated at atmospheric pressure using 0.10 g of 10% palladium of charcoal catalyst. After 2 hours, the solution was filtered through celite (filter acid) and the clear solution was concentrated down to give crystals from which 0.4 g of hexahydrobenzamide m.p. 184-186 C was isolated

by recrystallization; reported m.p. 185-186 C (29).

(C) Reduction of Benzenephosphonic Acid.

(I) First Attempted Reduction.

Twelve and six-tenth gram (0.08 mole) of benzenephosphonic acid (Eastman Kodak) was added to 600 ml of liquid ammonia which has been condensed in 2 liter three-necked flask equipped with a mechanical stirrer, a dropping funnel and a dry ice condenser. The solution stirred while 4.5 g (0.64 mole) of lithium was added in small pieces over 20 minutes. Then 100 ml of anhydrous ethanol was added over a period of 40 minutes with stirring, followed by addition of 34.5 g (0.64 mole) of ammonium chloride. The ammonia was allowed to evaporate and the residual material was dissolved in 100 ml of ice water. After acidification with 10% hydrochloric acid, the solution was extracted with four 200 ml portions of ether. The combined ether solution was dried over magnesium sulfate. The ether solution was removed by distillation to give 11 gm of solid residue. This solid melted at 159° - 160° C. The original benzenephosphonic acid melts at 161° - 162° C. The solid residue was analyzed also by ultraviolet and infrared absorptions. Both spectrum indicated the compound is benzenephosphonic acid (90% recovery).

(II) Second Attempted Reduction.

Same quantities of reagents were used here as in experiment (I). This time ethanol was added first over 40 minutes. Then lithium was added in small pieces over 30 minutes, followed by ammonium chloride. The isolation procedure was described above. Distillation of ether gave only solid residue (10.7 g). Ultraviolet and infrared absorption indicated it was benzenephosphonic acid (85% recovery).

(III) Third Attempted Reduction.

The procedure was same as experiment (I) using 12.6 g (0.08 mole) of benzenephosphonic acid, 2.25 g (0.32 mole) lithium and 100 ml of ethanol. The etheral solution was concentrated in vacuum and the remaining liquid was distilled at 60° - 120° C. The distillate was analyzed by gas chromatography and was shown to be ether and ethanol with no other low boiling material. The solid residue was shown to be benzenephosphonic acid from spectral data.

(IV) Fourth Attempted Reduction.

Twelve and six-tenth gram of benzenephosphonic acid was added through dropping funnel to the 600 ml liquid ammonia with stirring for 30 minutes. Then 4.5 g (0.64 mole) of lithium was added in small pieces over 20 minutes. 100 ml ethanol was added slowly over 2½ hours, followed addition by 34.5 g of ammonium chloride. Isolation procedure was as

described in experiment (VI). 10.7 g of solid residue was isolated and was shown to be benzenephosphonic acid (85% recovery) from spectral data.

(V) Fifth Attempted Reduction.

Same quantities of reagents were used here as in previous experiment. This time, 300 ml tetrahydrofuran was used as co-solvent to dissolve benzenephosphonic acid. The rest procedure was same as before. Only solid residue (10.5 g) were isolated and was shown to be benzenephosphonic acid (83% recovery) from spectral data.

(D) Preparation of 1,4-dihydrobenzoic acid.

(I) Twenty gram (0.164 mole) of benzoic acid was added to 600 ml of liquid ammonia which had been condensed in a 2 liter three-necked flask equipped with a mechanical stirrer, a dropping funnel and a dry ice condenser. The solution was stirred while 200 ml absolute ethanol was added through dropping funnel over a 20 minutes period. Then 4 gm. (0.54 mole) lithium was added in small pieces over a hour with stirring, followed by addition of 29.6 g (0.54 mole) of ammonium chloride. The ammonia was allowed to evaporate and the residual material was dissolved in 300 ml of ice water. After acidification with 10% hydrochloric acid, the solution was extracted with four 100 ml portions of ether. The

combined ether solution was dried over magnesium sulfate. The ether solution was concentrated by distillation under vacuum to remove ether and ethanol. The remaining light yellow liquid weighted 16 g (80% yield). The ultraviolet absorption of this liquid showed 275 mu (E = 87); pure benzoic acid has (E = 800); thus indicated the presence of 10.6% of benzoic acid.

(II) Purification of 1, 4-dihydrobenzoic Acid by Means of S-benzylisothiuronium Derivative

One and seventy six-hundredth gram (0.014 mole) of 1, 4-dihydrobenzoic acid was dissolved in 10 ml of ethanol. Neutralization of the acid was achieved by adding 10% Na_2CO_3 to phenophthalein red. A hot solution of 4.24 g (0.21 mole) of beneylthioureahydrochloride in 10 ml ethanol was added to the former. The solution was cooled in refrigerator and a white precipitate formed which was isolated by filtration. The white precipitate (S-benzylisothiuronium salt) was recrystallized twice with ethanol. It melted at 146° - 147° D. Reported m.p. 148° C (27). Ultraviolet of this salt showed no absorption above 220 mu. This salt was then converted back to free acid by adding excess of dilute hydrochloric acid. The solution was immediately extracted with three 100 ml portions of ether. The combined ether solution was dried over magnesium sulfate. The solution was concentrated by

distillation under vacuum. The light yellow liquid remaining showed ultraviolet absorption at 275 mu (E = 31) which indicated presence of 3.8% benzoic acid.

(III) Phenylhydrazine Derivative of 1, 4-dihydrobenzoic acid.

Addition of 0.4 g (0.0038 mole) of phenylhydrazine to a solution of 0.5 g (0.004 mole) of the acid in 1.5 ml of benzene and cooling in ice gave the crystalline hydrazine salt m.p. 77-80 C. Recrystallized once with benzene m.p. 79-80 C, reported m.p. 80-81 C (28).

(IV) P-bromophenacyl derivative of 1,4-dihydrobenzoic acid.

Half gram (0.004 mole) of 1,4-dihydrobenzoic acid was dissolved in 10 ml ethanol in a 150 ml round bottom flask. It was neutralized with Na_2CO_3 (10%) to litmus blue. Two drops of dilute HCl was added to turn litmus red. 0.5 g (0.002 mole) p-bromophenacyl bromide was then added to the solution. The flask was then fitted with reflux condenser and the solution was refluxed under hot water bath for an hour, and cooled in ice. The crystals were induced by scratching with a spatula and recrystallized once with ethanol and water. m. p. 157° - 158° C.

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